Lowering the Risk of Visual Impairment and Blindness

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Diabetic retinopathy remains the leading cause of visual disability and blindness among professionally active adults in economically developed societies, which is of particular concern because the prevalence and incidence of Type 2 diabetes mellitus is expected to increase sharply during the next decade. Retinopathy is fundamentally similar in Type 1 and Type 2 diabetes mellitus, and it is widely accepted that if detected and treated early, loss of vision and blindness from diabetic retinopathy may be prevented. Studies such as the Diabetes Control and Complications Trial (DCCT), the United Kingdom Prospective Diabetes Study Group (UKPDS), the Diabetic Retinopathy Study (DRS) and the Early Treatment Diabetic Retinopathy Study (ETDRS) have established accepted guidelines for the management of diabetic retinopathy. Good metabolic control is particularly important in the early phases of the disease, and will delay the onset of retinopathy and decrease the rate of progression. When advanced stages of retinopathy are reached, laser photocoagulation is effective in decreasing the development to blindness by over 50 %. However, preventable blindness still occurs despite the tight control of blood glucose levels and the use of retinal photocoagulation. To reduce the risk of visual impairment and blindness caused by diabetes, diabetic patients must be taught how to control their blood glucose levels, regular eye examinations must be carried out and the conditions for timely laser photocoagulation must be created. The implementation of screening and treatment programmes for visual impairment in diabetes has proved to be worthwhile in terms of costs and health benefits. © 1998 John Wiley & Sons, Ltd.

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Introduction

The long-term complications of diabetes are the most costly aspect of the disease to both the individual and society in general. However, considerable scope for the prevention of diabetic complications exists; indeed, visual impairment and blindness caused by diabetic retinopathy may be prevented by early detection and intervention with laser therapy. Diabetic retinopathy is the leading cause of visual disability and blindness among professionally active adults aged 20–64 years in economically developed societies and therefore preventive strategies are particularly relevant.[1] Preventive programmes are particularly important because a sharp increase in the prevalence and incidence of diabetes, especially Type 2 diabetes, is expected in the next decade. The major focus of attention on insulin-dependent diabetes or Type 1 diabetes has distracted healthcare providers in previous years from paying attention to non-insulin-dependent diabetes or Type 2 diabetes, a more insidious form of diabetes that is threatening to become a pandemic. Whereas Type 1 diabetes may ultimately affect 0.5 % of the entire population, Type 2 diabetes is predicted to affect almost 10 % of the world population by the year 2000.[2]

Epidemiological Data

Most available data on the epidemiology of diabetic retinopathy have major shortcomings, particularly the lack of well controlled population studies. However, three such studies have been carried out that may be considered informative enough to shed some light on this subject. Two have been performed in Europe (Sweden and Denmark)[3–5] and one (the most complete) in the USA.[6,7] The results of these studies are generally in agreement and show that the retinopathy in Type 1 and Type 2 diabetic patients is fundamentally similar in its progression and final consequences (Table 1). The retinopathy is usually more severe and more frequent in Type 1 diabetic patients, but because of the increased prevalence of Type 2 diabetes, more cases of macular oedema and proliferative retinopathy occur in Type 2 diabetic patients. If detected and treated early, visual impairment and blindness caused by diabetic retinopathy can be prevented.

Studies, such as the Diabetes Control and Complications Trial (DCCT),[8] the United Kingdom Prospective

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Table 1. Patients affected by diabetic retinopathy during a lifetime (%)

Retinopathy	Patients affected during lifetime (%)		Clinical manifestations
	Type 2 diabetes	Type 1 diabetes	
Mild	50–75	90	Minimal effect on vision
Severe	19–20	30–50	Legal or total blindness

Diabetes Study (UKPDS),[9] the Diabetic Retinopathy Study (DRS)[10] and the Early Treatment Diabetic Retinopathy Study (ETDRS),[11] validated methods now considered standard in treating diabetes when it occurs, i.e. tight control of blood glucose levels to prevent retinopathy and laser photocoagulation to halt progression after development of clinically significant macular oedema or proliferative retinopathy. These landmark studies clearly changed the expected outcomes of diabetic retinopathy by offering effective approaches to its management.

The DCCT, which involved Type 1 diabetic patients, showed that intensive therapy delayed the onset of retinopathy and slowed the progression of existing retinopathy, and that tight metabolic control markedly reduced the risk of visual impairment and blindness.[8] However, the DCCT also made clear that some patients achieving good glycaemic control still have extensive secondary complications. An intervention study of Japanese Type 2 diabetic patients[12] reported a 6-year cumulative development and progression in retinopathy of 7.7 % in the intensively treated group (mean HbA_{1c} 7.1 %) compared with 32 % in the conventionally treated group (HbA_{1c} 9.4 %), confirming the beneficial effect of tight glycaemic control. More recently, the UKPDS showed that intensive blood glucose control by either sulphonylureas or insulin substantially decreases the risk of microvascular complications.[9] The ETDRS is a 19-year project funded by the National Eye Institute (NEI) to examine the management of Type 1 and Type 2 diabetic patients with non-proliferative or early proliferative diabetes retinopathy using photocoagulation.[11] The ETDRS confirmed the effectiveness of treating microaneurysms and leaking lesions with photocoagulation, which is now the leading treatment to preserve vision in diabetic macular oedema. The NEI recently started a 10-year follow up of a cohort of patients from the ETDRS with the long-term aim of investigating the value of photocoagulation in preserving and maintaining vision. From the DRS, researchers found that photocoagulation decreased the risk of severe vision loss by at least 50 % in both types of diabetic patients with proliferative retinopathy.

As a result of these large clinical trials, well established guidelines for the management of diabetic retinopathy now exist. Good glycaemic control that maintains low blood glucose levels is important, particularly in the earliest phases of the disease, and can delay the onset of retinopathy and slow its progression. The UKPDS has also shown that tight blood pressure control in patients with hypertension and Type 2 diabetes achieves a clinically important reduction in the progression of diabetic retinopathy.[13] Once the diabetic retinopathy is established and advanced stages of the disease with visual loss are reached, laser photocoagulation is effective in reducing the development to blindness by over 50 %. Photocoagulation and good glycaemic control are important improvements in the management of diabetic retinopathy, which is clearly more beneficial than 15 years ago. However, despite the aim of tight control of blood glucose and the use of retinal photocoagulation, preventable blindness still occurs. Only approximately 50 % of people with diabetes have an eye examination carried out each year and many patients with diabetes are not able to achieve tight glycaemic control. Furthermore, photocoagulation remains a relatively poor treatment alternative since it is an invasive technique, which achieves results by destroying the retina. Other forms of therapy targeted at the earliest stages of retinal disease, when the disease process may still be reversible and before visual loss is present, are urgently needed.

How to Reduce the Risk of Visual Impairment and Blindness

Firstly, the present guidelines for management of diabetic retinopathy, even with their shortcomings, should be applied to all patients with diabetes. Educating diabetic patients plays a vital role in managing the disease (Table 2). For the patient with diabetes, the key to maintaining good health is controlling the level of glucose in the blood. Information, education and self-discipline are therefore required for effective disease management, which is particularly important in Type 1 diabetes immediately after puberty, at an age when acceptance of the disease is most difficult.

Table 2. To reduce the risk of blindness caused by diabetes

- Teach the diabetic patient to keep good glycaemic control
- Examine eyes regularly
- Improve chain of referral at all levels
- Patients must not wait for visual loss
- Physicians must not forget retinopathy
- Ophthalmologists must treat and follow up all cases

Secondly, regular eye examinations are fundamental. Existing clinical practice has not led to appropriate and regular eye screening of diabetic patients. Improvements must be made at all levels of the 'chain of referral', i.e. from patients to general practitioners, through to the diabetologist and eventually the ophthalmologist, if the aim of reducing the frequency of vision loss in the population is to be achieved. At present, the key to preventing visual disability is the identification and treatment of diabetic retinopathy and macular oedema before lesions progress to a high-risk status. Clearly, this is a role for an effective screening programme. Screening for diabetic retinal complications is accepted as a worthwhile undertaking in terms of health benefits. The cost-effectiveness of screening and treating diabetic retinopathy has been well demonstrated.[14,15]

Annual photographic screening of all diabetic patients after puberty followed by appropriate photocoagulation treatment when indicated has proven its value. Recently, Backlund *et al.*,[16] have shown that a prevention programme in Stockholm County (Sweden), which involved education, increased frequency of eye examinations and the establishment of a rapid referral and treatment system reduced the number of new cases of blindness caused by diabetes by 7 % per year. Clearly, the risk of visual impairment and blindness can be reduced, and strategies to prevent diabetic retinopathy should be rapidly implemented following the recommendations of the St. Vincent declaration.

However, the fight against blindness caused by diabetes is far from being won. Firstly, established knowledge of diabetic retinopathy should be applied more efficiently (Table 2). Patients should not wait until visual loss occurs to visit an ophthalmologist and, in this area, primary care physicians have a fundamental role in helping patients avoid this most serious mistake. The ophthalmologists should aggressively treat their patients with photocoagulation whenever clearly indicated and follow up closely. Retinal photocoagulation is not a one-time treatment and repeated treatments, sometimes at relatively short intervals, are needed frequently. Finally, the realization that hyperglycaemia is the direct factor responsible for the development of retinopathy is opening interesting perspectives for medical therapy and prevention of diabetic retinal disease.

Mechanisms and Prospects for Future Therapy

The retina as a neural tissue has relatively limited forms of response to injury. Recent findings in our laboratory have shown that the retinal vessels make the inner retina particularly susceptible to chronic hyperglycaemia. The abnormal accumulation of glucose in the retina in diabetes leads to increased lactate-to-pyruvate ratios and lactic acidosis. Expected associated changes include glutamate release and calcium excitotoxicity, which establishes a chain of events not entirely different from the ischaemia-reperfusion type of injury. A number of target sites may be chosen during these processes to halt retinal cellular damage and the subsequent vascular cell alterations with breakdown of the inner blood-retinal barrier, which trigger full diabetic retinopathy. Future medical therapy for diabetic retinopathy will probably involve the association of drugs acting at three levels. Tri-therapy for diabetic retinopathy should include: the medication necessary for best euglycaemic control (insulin or oral antidiabetic drugs); a second drug administered to correct the altered metabolism of the retina associated with the excess glucose availability (aldose reductase, protein kinase C inhibitors or antioxidants); and a third drug that acts as a neuroprotective or vasoprotective agent. The major concern, however, will be safety. Medical therapy of diabetic retinopathy may be initiated immediately after the diagnosis of diabetes and before visual loss and retinal lesions are irreversible, which results in long-term benefits. Side-effects should be minimal and the medication must have a good benefit-to-risk ratio to be accepted.[17,18]

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